AMENDMENTS

Please amend the Application as follows.

In the Title:

Please change the title to Method for Selectively Stimulating Proliferation of CD8+ T Cells.

In the Specification:

Please insert the enclosed Sequence Listing in paper form after the last page of the specification.

Please delete the paragraph at page 1, lines 3-4 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

METHODS FOR SELECTIVELY STIMULATING PROLIFERATION OF CD8+ T CELLS

Please delete the paragraph at page 1, lines 7-17 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

This application is a continuation application of U.S. Patent No. 5,858,358, issued on January 12, 1999, which in turn is a continuation-in-part of the following U.S. applications: U.S. Serial No. 08/073,223, filed June 4, 1993, entitled "Methods for Selectively Stimulating Proliferation of T cells"; U.S. Serial No. 07/864,805, filed April 7, 1992, entitled "CD28 Pathway Immunoregulation"; U.S. Serial No. 864,866, filed April 7, 1992, entitled "Enhancement of CD28-Related Immune Response"; and U.S. Serial No. 07/864,807, filed April 7, 1992, entitled "Immunotherapy Involving Stimulation of Th CD28 Lymphokine Production". The

contents of each of these applications is incorporated herein by reference.

Please delete the paragraph at page 3, lines 31-35 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

Figure 5 depicts fluorescent activated cell sorter analysis (FACS) in which cells were stained after isolation (day 0, Fig. 5A), or after 26 days in culture with either CD28 stimulation (Fig. 5B) or IL-2 culture (Fig. 5C), with phycoerythrin conjugated anti-CD3, CD4, CD8 or with an IgG2a control monoclonal antibody and fluorescence quantified with a flow cytometer.

Please delete the paragraph at page 3, lines 36 through page 4, line 2 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

Figure 6 shows FACS analysis of the EX5.3D10 monoclonal antibody depicting reactivity with CD28 in comparison to an anti-CD28 monoclonal antibody 9.3. The following cell lines were tested: Fig. 6A, untransfected CHO-DG44 cells; Fig. 6B, CHO-HH cells; Fig. 6C, unactivated peripheral blood lymphocytes; and Fig. 6D, Jurkat No. 7 cells.

Please delete the paragraph at page 4, line 3-6 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

Figure 7 shows FACS analysis of the ES5.2D8 monoclonal antibody depicting the binding reactivity with the following cell lines: Fig. 7A, CHO-DG44 cells; Fig. 7B, CHO-105A cells; Fig. 7C, unactivated human peripheral blood lymphocytes; and Fig. 7D, PMA activated peripheral blood lymphocytes.

Please delete the paragraph at page 5, line 1-3 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

Figure 18 show FACS analysis of the monoclonal antibody ES5.2D8 (Figs. 18C and D) or a control IgG (Figs. 18A and B) depicting the binding reactivity with MOP cells transfected with a plasmid encoding the CD9 antigen.

Please delete the paragraph at page 35, line 36 through page 36, line 9 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

Experiments were conducted to determine whether a population of $CD8^+$ T cells could be preferentially expanded by stimulation with an anti-CD3 mAB and a monoclonal antibody 2D8. $CD28^+$ T cells were obtained essentially as described in Example 1. To assay for CD8 expression, a primary anti-CD8 antibody and a labeled appropriate secondary antibody were used in FACS analysis to determine the percent positive cells. As shown in FIG. 17, at day 7 following stimulation of T cells with the anti-CD3 mAb G19-4sp and the mAb 2d8, the $CD8^+$ fraction had increased from approximately 20% to over 40%. Another

monoclonal antibody ER4.7G11 (referred to as 7G11) was also found to stimulate $CD8^+$ T cells. This antibody was raised against recombinant human CTLA4 and has been deposited with the ATCC on Jun. 3, 1994 at Accession No. HB11642. This result indicates that binding of either a distinct region of CTLA4 or of a cross-reactive cell surface protein selectively activates $CD8^+$ T cells.

Please delete the paragraph at page 57, lines 1-2 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

METHODS FOR SELECTIVELY STIMULATING PROLIFERATION OF CD8+ T CELLS

Please delete the paragraph at page 57, lines 6-14 of the specification and, in accordance with the provisions of 37 C.F.R. §1.121(b)(1)(i-ii), please replace the deleted paragraph with the following paragraph:

Methods for inducing a population of $CD8^+$ T cells to proliferate by activating the population of $CD8^+$ T cells and stimulating a CD9 accessory molecule on the surface of the T cells with a ligand which binds the accessory molecule are described. T cell proliferation occurs in the absence of exogenous growth factors or accessory cells. T cell activation is accomplished by stimulating the T cell receptor (TCR)/CD3 complex or the CD2 surface protein. To induce proliferation of an activated population of T cells, an accessory molecule on the surface of the T cells, such as CD28 or CD9, is stimulated with a ligand which binds the accessory molecule. The T cell population expanded by the method of the invention can be genetically transduced and